UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,046	02/20/2002	Jim Wells	SUNESIS.2DV1C2	9481

20995 7590 07/02/2003

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 07/02/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
File Copy	10/082,046	WELLS ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40,41,43,45-51,59 and 60* is/are pending in the application.

4a) Of the above claim(s) *59 and 60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40,41,43 and 45-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Application

1. The Response filed April 18, 2003 (Paper No. 7) is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 40-63 were pending. The Examiner withdrew claims 44 and 52-63 in Paper No. 5 as being drawn to non-elected inventions and/or species. Applicants' amended claims 40 and 59 and cancelled claims 42, 44, 52-58 and 61-63 in Paper No. 7. Therefore, claims 40-41, 43 and 45-51 are examined on the merits in this Action.

Election/Restriction

4. Applicants submit that the prior art cited by the Examiner does not anticipate or render obvious the elected species, accordingly, it is anticipated that, under the provisions of MPEP § 803.02, the search will be extended to the non-elected species, and the genus claims will be allowed within the full scope of the claims currently pending.

5. Please note that Applicants' elected species (see Response to Restriction Requirement, Paper No. 4) were found in the art, see Paper No. 5 and new rejections below. Applicant is reminded of MPEP § 803.02 with respect to species elections.

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to ***the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final.*** Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

IDS

6. The references listed on applicant's Supplemental PTO-1449 (Paper No. 8) form have been considered by the Examiner. A copy of the form is attached to this Office Action.

Withdrawn Objections/Rejections

7. The rejection under the first paragraph of 35 U.S.C. 112 denoted "New Matter" is hereby withdrawn in view of Applicants' arguments and/or cancellation of claim 42. The rejection under 35 U.S.C. 102(b) by Erlanson et al is hereby withdrawn in view of Applicants' arguments and/or cancellation of claim 42. The rejections under 35 U.S.C. 103(a) are hereby withdrawn in view of Applicants' arguments and/or amendments and/or cancellation of claims. The Double Patenting Rejections are hereby withdrawn in view of Applicants' submission of a Terminal Disclaimer (see below).

Outstanding Objections and/or Rejections

Double Patenting

8. The terminal disclaimer filed on April 18, 2003 disclaiming the terminal portion of any patent granted on this application that would extend beyond the expiration date of U.S. Patent No. 6,335,155 has been reviewed and is accepted. The terminal disclaimer has been recorded.

New Rejections

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 40-41, 43 and 45-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Pitner et al (U.S. Patent No. 5,367,058) (Date of Patent is **November 22, 1994**) (see supplemental IDS, Paper No. 8).

For ***claims 40-41, 43 and 45-46*** Pitner et al (see entire document) discloses a method for modifying antibodies, which anticipates claims 40-41, 43. For example, Pitner et al discloses a method for identifying various non-oligomeric ligand (PC, PC-MAL, PC-CHO, PC-TP, GlcNAc-CHO, GlcNAc-MAL, see figures 1-12) to a target protein (McPC603, SH-McPC603, st9, modified st9, see figures 1-12) wherein said

ligand is less than about 750 daltons (PC, PC-MAL, PC-CHO, PC-TP, GlcNAc-CHO, GlcNAc-MAL are all less than 750 daltons, see figures 1-12) wherein the method comprises [a] obtaining said target protein comprising a –SH group, masked SH group, or activated –SH group (see figure 1 showing target McPC603 protein with a free –SH group), [b] contacting said target protein with one or more non-oligomeric ligand candidates wherein said ligand candidates each comprises a disulfide bond (see figures 2 and 6 showing the ligand PC-TP that contains a disulfide bond being contacted with the candidate protein McPC603-SH), [c] forming a covalent target protein-ligand conjugate wherein at least one ligand candidate binds to the target protein and forms a disulfide bond with the target protein under disulfide exchange conditions (PC-TP forms a covalent bond with McPC603 via a disulfide exchange, see figure 6; see also columns 2-4; see also Examples 2-4; see especially column 6, lines 11-14, "The increase in affinity of the thiol modified antibody (both McPC603 and St9) is presumed to be due to the formation of a disulfide bond with the free thiol of the modified antigen [i.e., disulfide exchange]"), [d] detecting the formation of said covalent target protein-ligand conjugate with the target protein under disulfide exchange conditions (see figures 10-12 showing UV detection at 492 nm; see also Examples 4 and 9).

For **claims 45-46**, Pitner et al discloses dithiothreitol (DTT) (see Pitner et al, figures 5 and 10; see also Examples).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 40-41, 43 and 45-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pitner et al (U.S. Patent No. 5,367,058) (Date of Patent is **November 22, 1994**) (see supplemental IDS, Paper No. 8) and Siuzdak (Siuzdak, G. Mass Spectrometry for Biotechnology. New York: Academic Press. **1996**, pages 119-126).

For ***claims 40-41, 43 and 45-46***, Pitner et al teaches all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates claims 40-41, 43 and 45-46 and, consequently, also renders obvious claims 40-41, 43 and 45-46.

The prior art teachings of Pitner et al differ from the claimed invention as follows:

For **claims 47**, Pitner et al is deficient in that although it teaches the use of DTT as a reducing agent, it does not specifically teach the use of 2-mercaptoethanol as the reducing agent. However, any reducing agent commonly used would have been obvious including 2-mercaptoethanol because each would have the same effect and the final decision would ordinarily be determined on cost and availability of the reagents.

For ***claims 48-51***, Pitner et al is deficient in tat it does not specifically teach the use of mass spectrometry.

However, Siuzdak teaches the following limitations that are deficient in Pitner et al:

For ***claim 48-51***, Siuzdak (see entire document) teaches the use of electrospray mass spectrometry to study both "non-covalent" and "covalent" antibody-antigen interactions including fragmentation techniques like MS^2 and MS^3 (see pages 119-126, especially figures 6.3-6.6 and Table 6.1).

It would have been obvious to one skilled in the art at the time the invention was made to "identify" antibody/antigen interactions using the method steps as taught by Pitner et al in conjunction with the mass spectrometer techniques as taught by Siuzdak because Siuzdak explicitly shows that the technique can be applied to both "covalent" and "non-covalent" antibody-antigen interactions (see Siuzdak, figures 6.3, 6.5; see especially paragraph bridging pages 125-126, "Electrospray mass spectrometry has also demonstrated its potential in the analysis of noncovalent interactions between an antibody and a hapten, and for observing covalent protein-bound intermediates in an antibody-

catalyzed reaction"), which would encompass the "antibody-antigen" complexes of Pitner et al. Furthermore, one of ordinary skill in the art would have been motivated to use the mass spectrometers as taught by Siuzdak with the antibody-antigen conjugates as taught by Pitner et al because Siuzdak explicitly states that electrospray has "demonstrated its potential" for these systems (see Siuzdak, page 126, paragraph 1).

Furthermore, one of skill in the art would be especially motivated to use mass spectrometry as disclosed by Siuzdak et al with the "antibody-antigen" complexes as described by Pitner et al because Siuzdak et al discloses that BOTH "covalent" and "non-covalent" interactions can be measured (and distinguished) using a mass spectrometer (see Siuzdak et al, page 123, paragraph 3, "Declusterin potentials on the order of 70 V or greater usually promote the dissociation of noncovalent complexes as well as covalent fragmentation, while lower potentials (<70 V) are conducive to the observation of noncovalent complexes (protein complexes have been analyzed at declustering potentials of 40 V). In order for the method of Pitner et al to work the modified antibodies must bind "covalently" to their respective antigens (see Pitner et al, figure 1 disclosing the covalent attachment of an antigen to a sulfhydryl group on the modified antibody). Therefore, any analytical technique that can confirm the "covalent" attachment of the antigen to the modified antibody is particularly useful. Consequently, a person of skill in the art would be motivated to "identify" even a "known" ligand using a mass spectrometer to determine the type of interaction (i.e., covalent v. non-covalent) to ascertain whether the modified antibody is truly able to bind to its respective antigen via a "covalent" bond as required by the method (as opposed to an induced conformational

change in the antibody that might increase the normal antibody-antigen binding interactions via a "non-covalent" interaction). Consequently, a person of skill in the art would be motivated to search for the "modified" antigens as disclosed by Pitner et al (e.g., PC-MAL, see figure 3 containing different linkers and binding groups) with electrospray mass spectroscopy as disclosed by Siuzdak et al to find modified antigens that can "covalently" bind to the antibodies as opposed to any unwanted "non-covalent" interactions that might occur.

Finally, one of ordinary skill in the art would have reasonably expected to be successful because Siuzdak shows many examples of enzyme-ligand interactions that have successfully been analyzed on a mass spectrometer (e.g., see figures 6.3 and 6.5).

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D. Epperson, Ph.D. whose telephone number is (703) 308-2423. The examiner can normally be reached on Monday-Thursday from 9:30 to 7:00 and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of

a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jon D. Epperson, Ph.D.
June 28, 2003

BENNETT CELSA
PRIMARY EXAMINER